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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/203,078	12/01/1998	SHUYUAN ZHANG	INRP:081	3754

7590 06/03/2004

STEVEN L. HIGHLANDER  
FULBRIGHT & JAWORSKI L.L.P.  
600 CONGRESS AVENUE, SUITE 2400  
AUSTIN, TX 78701

EXAMINER

FOLEY, SHANON A

ART UNIT	PAPER NUMBER
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1648

DATE MAILED: 06/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<p align="center"><b>Office Action Summary</b></p>	<b>Application No.</b> 09/203,078	<b>Applicant(s)</b> ZHANG ET AL.	
	<b>Examiner</b> Shanon Foley	<b>Art Unit</b> 1648	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 08 March 2004.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-62 is/are pending in the application.
- 4a) Of the above claim(s) 33-37 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-32 and 38-62 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |  |
|--|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)<br>2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)<br>3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____. | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____.<br>5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)<br>6) <input type="checkbox"/> Other: _____. |
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### **DETAILED ACTION**

In the amendment submitted March 8, 2004, applicant amended claims 1-3, 18, 29 and added new claims 30-62. Claims 1-62 are pending.

Upon further consideration of the claims and the prior art and a reconsideration of the declaration under 37 CFR 1.132 by Shawn Gallagher submitted February 28, 2002, it is determined that new grounds of rejection are required.

#### ***Election/Restrictions***

Newly submitted claims 33-37 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: The claims encompass administration of the adenovirus. The subject matter of the claims under examination is drawn to a process of preparing an adenovirus. The active steps of administering in new claims 33-37 do not further limit steps of preparing. Therefore, the subject matter encompassed by claims 33-37 are beyond the scope of the originally presented claims.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 33-37 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 1-32 and 38-62 are under consideration.

#### ***Priority***

From the "Remarks" section, applicant appears to intend the first line of the specification to disclaim benefit of priority to parent applications. However, the actual amendment to the specification cites page 3, instead of page 2. Therefore, while the examiner acknowledges the

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cancellation of priority, an appropriate correction to the amendment of the specification is required. In view of the amendment of the priority claimed, the effective date of the instant application is the filing date, December 1, 1998.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 32 and 48 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 32 is incomprehensible. Is the pharmaceutically acceptable composition different from the pharmaceutically acceptable carrier?

It cannot be determined if the improvement of claim 48 requires the improvement of claim 47 or not. It is presumed that the improvement recited in claim 48 is additional to the limitations of claim 47. However, this presumption does not relieve applicant of the necessity to clarify the intended limitations of the claim. This rejection could be obviated by the insertion of "further" after "improvement" in line 1.

***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

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provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Since the priority date of this application has changed, US 2002/018723 A1 is now available as prior art since the subject matter claimed in US 2002/018723 A1 is supported in an application with a filing date of November 20, 1997.

Claims 1, 3-29, 38 and 47-62 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-29 of copending Pre-grant Publication Patent Application No. US 2002/018723 A1. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims encompass preparing a recombinant adenovirus, as evidenced by claim 38 for example. The remaining limitations between the instant claims and the pre-grant application publication are the same.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an

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international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 3, 8, 9, 13-25, 31, 32, 38, 47, 49 and 51-62 are rejected under 35 U.S.C. 102(b) as being anticipated by Huyghe et al. (Human Gene Therapy. 1995; 6: 1403-1416) in light of Kuchler, previously provided by applicant.

Applicant reiterates the broadest claim on page 12 and asserts that the summary provided is incorrectly characterized. Applicant's reiteration of the claim is appreciated, but the summary of the rejected claims starting on page 2 of the previous Office action includes the limitations of several claims for the sake of efficiency and succinctness. The teaching of a more limiting factor in the prior art of the claims necessarily teaches the broader concepts in less limiting claims. Therefore, the collection of claims anticipated by Huyghe et al. are summarized as follows:

The claims are drawn to a process of preparing adenovirus by preparing a culture of producer cells essentially homogenous with respect to growth, infecting the producer cells with adenovirus between mid-log and stationary phase, and harvesting the adenovirus and placing the virus into a pharmaceutically acceptable composition. The cells are allowed to attach to a surface between 3 and 24 hours prior to infection and are recirculated during infection. The adenovirus is replication-defective, lacking a portion of E1, which is complemented by 293 cells, and encodes the p53 gene from a CMV promoter. The adenovirus is purified by only one or several chromatographic separations including ion-exchange chromatography.

Huyghe et al. anticipate preparing adenovirus by preparing a culture of 293 producer cells that have attained an essentially homogenous confluency of 50-60% when the cells are infected with a replication-defective adenovirus expressing p53 from a CMV promoter in place of E1

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coding sequences. This percentage of confluency reasonably corresponds to mid-log phase of cell growth (explained in greater detail below). The 293 cells are allowed to attach to the surface between 2 and 2.5 days prior to infection and upon infection, the virus was mixed thoroughly with the cell culture medium. The adenovirus is harvested and added to phosphate-buffered saline supplemented with 2% sucrose and 2 mM  $\text{MgCl}_2$ , a pharmaceutically acceptable carrier. The adenovirus of Huyghe et al. is purified by several methods of chromatography, including ion-exchange chromatography. See the first full paragraph of the second column on page 1403, "Production of infected ATCC 293 cells", "Harvest and lysis", "Preparation of ACN53 standard material" and "Chromatographic parameters" bridging pages 1404-1405.

In the response and the declaration by Shawn Gallagher submitted February 28, 2002, applicant assumed seeding densities of Huyghe et al. and provided reasons for how the assumed seeding densities would be consistent the early log phase of growth. However, the Freshney reference and the Mediatech Technical Information provided with the declaration clearly indicate a number of factors contributing to the length of the log phase, which include seeding density and changes in the growth medium, see "The Log Phase" of Freshney on page 239 and "Growth Phases" in Mediatech Technical Information. Since seeding density is established in the art as a crucial component of the log phase and Huyghe et al. has not provided any information regarding the initial density of cells, applicant's presumption of early log phase density for the cells of Huyghe et al. is speculative and unsubstantiated.

When applying the teachings of Freshney to the cell density of Huyghe et al., applicant reasoned that the cells of Huyghe et al. would not be in late log phase and the examiner agrees.

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With respect to the teachings of Mediatech's Technical Information, applicant equates 70% confluency with log phase and reasons that 50%-60% confluency is only in early log phase at the very most. However, applicant appears to have misinterpreted the reference. While the reference indicates that cultures that are 70% confluent are in log phase, there is no differentiation between the various stages of log growth and % confluency provided by the reference. Therefore, applicant's conclusion that 50-60% confluency equates to early log phase is unsupported.

Finally, when the teachings of Kuchler are applied to the cells of Huyghe et al., applicant determines that the cells of Huyghe et al. are barely out of lag phase since the lag times of 293 cells ranges between 24-48 hours and Huyghe et al. infected the cells between 48 and 60 hours after seeding. Therefore, the supported facts provided by the references and the declaration are:

- 1) the lag time of 293 cells ranges between 24-48 hours
- 2) the cells of Huyghe et al. are have a confluency of 50-60% upon infection
- 3) the cells of Huyghe et al. attach to the surface of the plate for 48 to 60 hours before infection, which is beyond the hours required for the lag phase
- 4) the chart provided by Kuchler indicates that the growth curve of cells after 60 hours of incubation is the mid-point of the growth curve, i.e. mid-phase.

Therefore, from the factual evidence available, it is determined that the cells of Huyghe et al. are at mid-phase upon infection.

Claims 1, 3-9, 13-28, 30-32, 38-49 and 51-62 are rejected under 35 U.S.C. 102(a) as being anticipated by Zhang et al. (WO 98/22588), as further evidenced by Wu et al. (US 6,689,600 B1).



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Claims 1, 3-9, 13-28, 30-32, 38-49 and 51-62 are rejected under 35 U.S.C. 102(e) as being anticipated by Zhang et al. (US Patent No. 6,194,191 B1), as further evidenced by Wu et al. (US 6,689,600 B1).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Since the priority date of the instant application has changed to December 1, 1998, the disclosures of Zhang et al. (WO 98/22588, published May 28, 1998) and US (6,194,191, which enjoys the benefit of priority to November 20, 1996) are currently available as prior art. Since the disclosures of WO 98/22588 and US 6,194,191 are identical, only citations from the US patent are cited in the rejection in the interest of efficiency.

See the summary of claims 1, 3, 8, 9, 13-25, 29, 31, 32, 38, 47, 49 and 51-62 above. Claims 4-7, 10-12, 26-28, 30, 39-46 and 48 state that the culture cells are perfused for at least a portion of the time at a rate that maintains glucose levels between 1 and 1.5 gm of glucose/liter. The cells are lysed by means other than freeze-thaw. The producer cells are cultured in a various systems including a microcarrier, multiplate, perfused packed bed reactor, microencapsulation or bioreactors, such as stirred tank, airlift or sparge.

Zhang et al. anticipate a process of preparing adenovirus by preparing a culture of producer cells essentially homogenous with respect to growth, infecting the producer cells with

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adenovirus between mid-log and stationary phase, and harvesting the adenovirus and placing the virus into a pharmaceutically acceptable composition. Although Zhang et al. do not specifically teach "mid-log", the cells are determined to be at least mid-phase based on the 80-90% confluence and the types of conditions the cells are cultured in. In addition, Wu et al. provides a summary of the teachings of Zhang et al. and teaches that the cells of Zhang et al. are infected after mid-phase, see column 6, lines 18-34. The cells are allowed to attach to a surface between 3 and 24 hours prior to infection and are recirculated during infection. The adenovirus is replication-defective, lacking a portion of E1, which is complemented by 293 cells, and encodes the p53 gene from a CMV promoter. The adenovirus is purified by only one or several chromatographic separations including ion-exchange chromatography. In addition, Zhang et al. anticipate glucose levels during perfusion between 0.7 and 1.7 g/L and lysing the cells by autolysis or detergent. Zhang et al. also anticipate culturing the producer cells in various systems including a microcarrier, multiplate, perfused packedbed reactor, microencapsulation or bioreactors, such as stirred tank, airlift or sparge. See claims column 9, line 43 to column 16, line 49, column 40, line 49 to column 57, line 13 and claims 1-5, 9, 11-18, 20, 21, 28, 29, 30-39, 41-45, 61-63, 66, 68, 70-72, 77-80, 86 and 89.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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Claims 10-12 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Huyghe et al. as applied to claims 1, 3, 8, 9, 13-25, 31, 32, 38, 47, 49 and 51-62 above **or** Zhang et al. (WO 98/22588) **or** Zhang et al. US (6,194,191) as applied to claims 1, 3-9, 13-28, 30-32, 38-49 and 51-62.

The claims are drawn to specific seeding densities of the producer cells and particular characteristics of the harvested adenovirus.

Although none of the references, in the alternative, teach the specific cell numbers to be plated, the number would be a subjective determination by one of ordinary skill based on many factors, such as the type of cell, the condition of the cells before plating, and the nature of the cell's division, ect. Therefore, it would be prima facie obvious for one skilled in the art to determine the appropriate number of cells to plate for each situation encountered.

Further, although none of the references, in the alternative, teach a harvested adenovirus with the characteristics listed in claim 29, all of the references teach various methods of improving the quantity and/or purity of the recombinant virus obtained. Therefore, it would have been prima facie obvious to one of ordinary skill to test any one of the properties listed to ensure a good yield of adenovirus.

Claims 2 and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Huyghe et al. as applied to claims 1, 3, 8, 9-12, 13-25, 29, 31, 32, 38, 47, 49 and 51-62 above **or** Zhang et al. (WO 98/22588) **or** Zhang et al. US (6,194,191) as applied to claims 1, 3-32, 38-49 and 51-62 and further in view of Graham et al. (C31 of IDS) and Leu et al. (6,194,210 B1).

Claims 2 and 50 require that the cells are infected in late-log and stationary phase of growth.

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See the teachings of Huyghe et al. or either Zhang et al. reference in the alternative.

None of the references specifically teach infecting at late-log to stationary phase of cell growth.

As stated in the previous Office action, Leu et al. teach a method of producing large quantities of virus by allowing uniform attachment of cells, growing the cells to late-log phase with medium replenishment to provide adequate cell nutrition and infecting the cells at late-log phase and harvesting the virus, see column 11, lines 18-column 12, line 9 and claims 1 and 4. One of ordinary skill in the art at the time the invention as made would have been motivated to have propagated the adenovirus of Huyghe et al. or either Zhang et al. reference with the cell culture method steps of infection of Leu et al. to increase the amount of adenovirus produced in cell culture. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of growing the adenovirus of Huyghe et al. or either Zhang et al. reference with the cell culture method steps taught by Leu et al. because Leu et al. teach that a wide range of viruses may be propagated to generate vaccines using the method steps, see column 5, lines 29-32. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art, absent unexpected results to the contrary.

Applicant argues that Leu et al. is replete with references to hepatitis A and argues that the ordinary artisan would not turn to Leu et al. for method steps to culture adenovirus. Applicant provides a detailed discussion of the differences between hepatitis A and adenoviruses. Applicant also argues that the wide range of viruses mentioned in Leu et al. do not belong to the same family as Adenoviridae.

Applicant's arguments as well as the declaration of Shuyuan Zhang have been fully considered, but are found unpersuasive. As applicant has pointed out, the method of viral

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propagation taught by Leu et al. is clearly applicable to a wide range of unrelated virus families. Therefore, the teachings of Leu et al. are clearly a teaching applicable to the general viral propagation art.

Applicant also argues that Leu et al. do not teach any benefit of infecting cells at a particular time frame. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

In the instant case, it has been clearly demonstrated above that Huyghe et al. or either Zhang et al. reference anticipate infecting cells at mid-log phase. Leu et al. specifically teach infecting at late log phase and provide a clear motivation, i.e., to produce large quantities of virus. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for combining the teachings of Leu et al. with Huyghe et al. or either Zhang et al. reference not only because the method of Leu et al. is applicable to general viral propagation, but also because the primary references teach infection of adenovirus at least at mid-log phase. Further, Mediatech's Technical Information demonstrate that cells of at least 70% confluency are in log-phase. Therefore, cell confluency of 80-90% at the time of infection would certainly be at late-log phase. Graham et al. (reference C31 of the IDS) teaches infecting cells at 80-90% confluency with adenovirus, see section 3.1.2 on page 117. Graham et al. clearly

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demonstrate that the teachings of Leu et al. are applicable to adenovirus infection in cells at late-log phase of growth. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art, absent unexpected results to the contrary.

Claims 26-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Huyghe et al. as applied to claims 1, 3, 8, 9-12, 13-25, 29, 31, 32, 38, 47, 49 and 51-62 above, and further in view of Graham et al. (C7) for reasons of record.

Applicant argues that Graham et al. do not cure the deficiencies in the primary references. However, there are no deficiencies to cure. Therefore, the rejection is maintained for reasons of record. Further, it is noted that autolysis would be a conventional alternative to detergent lysis.

Claims 4, 30, 39-46 and 48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Huyghe et al. as applied to claims 1, 3, 8, 9-12, 13-25, 29, 31, 32, 38, 47, 49 and 51-62 above, and further in view of Garnier et al. (C26) and Spier et al. (C35 of the IDS) .

The claims require the producer cells to be perfused for a portion of the time the cells are cultured. The claims also require the cells to be cultured in various systems including a microcarrier, multiplate, perfused packbed reactor, microencapsulation or bioreactors, such as stirred tank, airlift or sparge.

Huyghe et al. do not teach perfusion or the various culture systems recited.

However, Garnier et al. teach scale-up adenovirus growth using medium replacement for controlling glucose concentrations for improved virus yields in a bioreactor, see the material and methods section. One of ordinary skill in the art at the time the invention was made would have been motivated to used the system of Garnier in the method of Huyghe et al. to produce larger quantities of adenovirus. One of ordinary skill in the art at the time the invention was made

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would have had a reasonable expectation of success in combining the teachings of Garnier et al. and Huyghe et al. because both references culture 293 cells for the propagation of adenovirus.

Neither Huyghe et al. nor Garnier et al. teach the various culture systems claimed. However, Spier et al. review each of the various culture systems claimed, see the entire reference. One of ordinary skill in the art at the time the invention was made would have been motivated to use a conventionally applied culture system, described by Spier et al. in the method and system of Huyghe et al. and Garnier et al. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success in using any of the culture systems of Spier et al. in the method of Garnier et al. and Huyghe et al. because Garnier et al. use a bioreactor system to propagate large quantities of adenovirus and Spier et al. review various types of bioreactor systems. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art, absent unexpected results to the contrary.

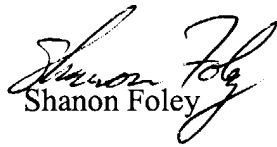
### ***Conclusion***

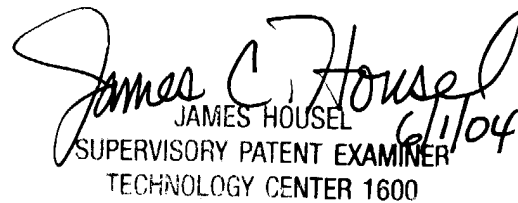
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon Foley whose telephone number is (571) 272-0898. The examiner can normally be reached on M-F 9:30 AM - 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
Shanon Foley

  
JAMES HOUSEL  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1600  
6/1/04